

FIG. 1A

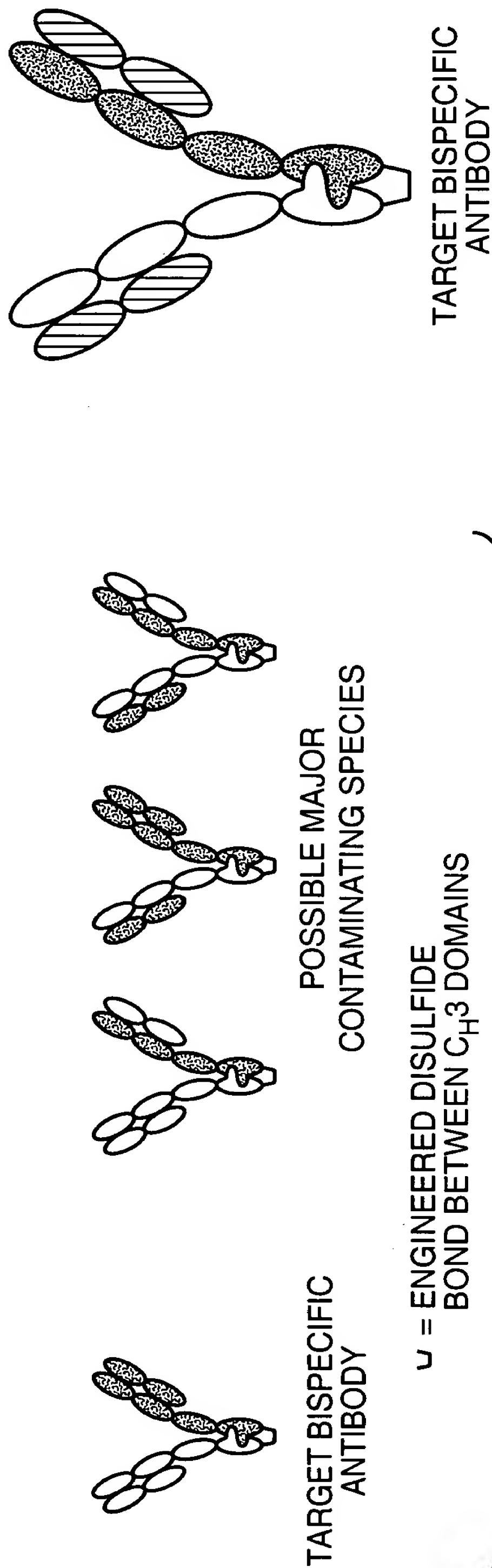


FIG. 1B

FIG. 1C

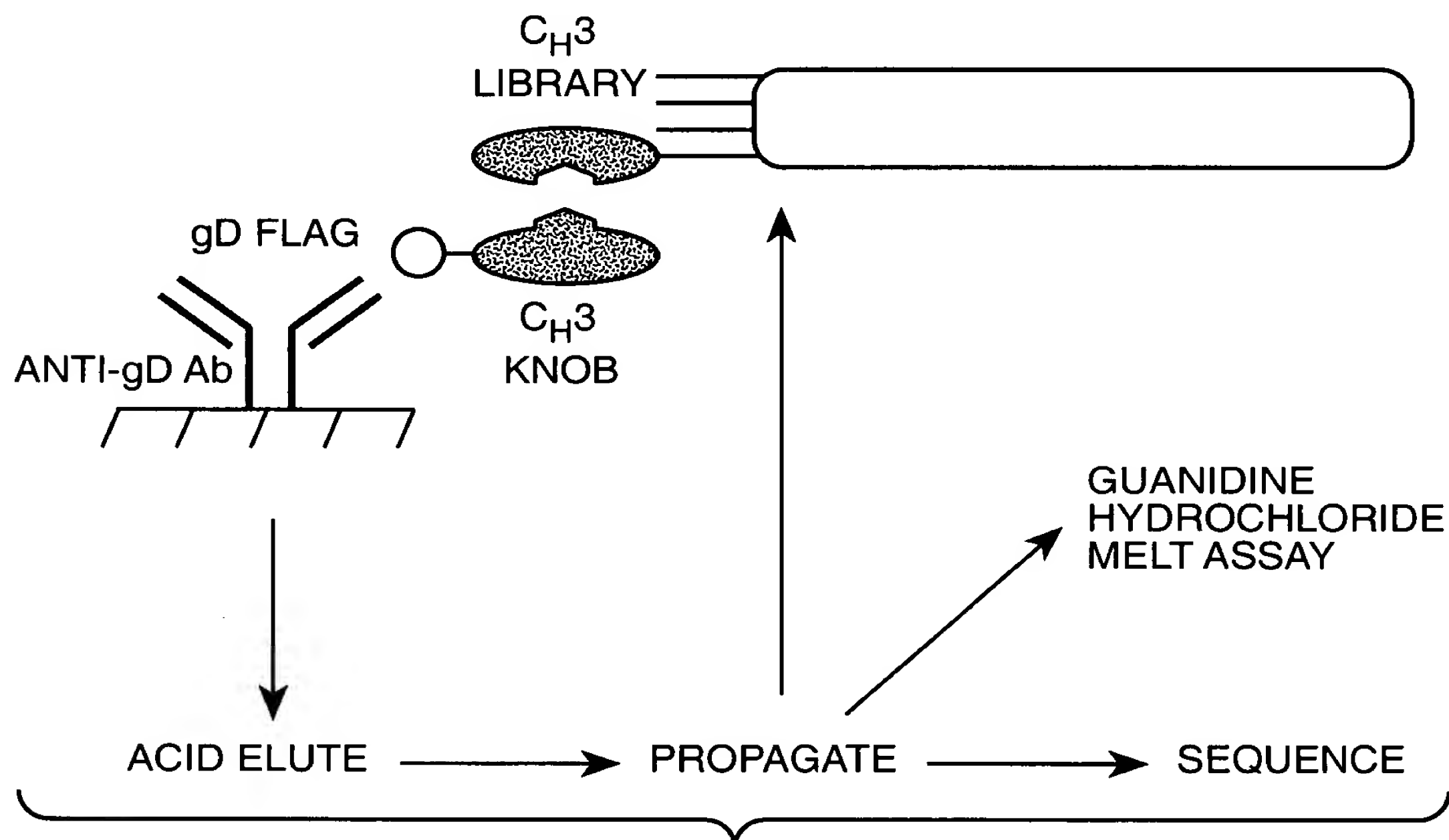


FIG. 2A



FIG. 2B

FIG. 2C-1

FIG. 2C-2

FIG. 2C

FIG. 2C-1

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stII      -> gD flag      -> G site      -> CH3
N  A  Y  A  L  K  M  A  D  P  N  R  F  R  G  K  D  L  A  A  H  Y  G  Q  P
AACGCGTACGCTCTGAAATGGCGGACCCGAACCGTTTTCGTGGTAAAGATCTGGCTGCACACTACGGCCAGCCG
MluI
R  E  P  Q  V  Y  T  L  P  P  S  R  E  E  M  T  K  N  Q  V  S  L  W  C  L
CGGGAACCTCAGGTGTATACCCCTGCCACCGTCTCGAGAAGAAATGACTAAACCAGGTCTCTGTGTGCTG
370                                     380                                     390
V  K  G  F  Y  P  S  D  I  A  V  E  W  E  S  N  G  Q  P  E  N  N  Y  K  T
GTCAAAGGTTTCTATCCGAGCGGATATCGCCGTGGAATGGGAAAGCAACGGTCAACCGGAAACAACTACAAACC
400                                     410                                     225
T  P  P  V  L  D  S  D  G  S  F  F  L  Y  S  K  L  T  V  D  K  S  R  W  Q
ACTCCACCGGTGCTGGATTCTGATGGCTCCTTCTTCTGTATTCTGAAGCTGACCGTTGACAAAGCCGTTGGCAG
300
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420                               430                               440
Q G N V F S C S V M H E A L M N H Y T Q K S L S L
CAAGGCAACGTTTTCAGCTGTTCTGTATGCACGAGGCCCTTGCAACCACTACACCCAGAAAGCCTGTCCCTG
375
S P G K O                               M K K N I A F L L
TCTCCCGGAAATAAGCTGAGGCTCCTCTAGAGGTGAGGTGATTTATGAAAAAGAAATATCGCATTTCTTCTTG
450
-> stII
350
A S M F V F S I A T N A Y A G Q P R E P Q V Y T L
CATCTATGTTTCGTTTTCCTATTGCTACAAACGCGTACGCTGGCAGCCCCGAGAACCAACAGGTGTACACCCCTGC
525
-> CH3
360 366 368 370
P P S R E E M T K N Q V S L Y C L V K G F Y P S D
CCCCATCCCGGAAGAGATGACCAAGAACCAAGCTTGTACTGCTGGTCAAGGCTTCTATCCCCAGCGACA
600
HindIII
380 390 400
I A V E W E S N G Q P E N N Y K T T P P V L D S D
TCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCAAGCCTCCCGTGTGGACTCCGACG
675
407 410 420
G S F F L Y S F L T V D K S R W Q Q G N V F S C S
GCTCCTTCTCCTCTACAGCTTTCACCGTCGACAAAGAGCAGGTGGCAGCAGGGGAACGCTTCTCATGCTCCG
750
SalI
430 440
V M H E A L H N H Y T Q K S L S L S P G K Am G P
TGATGATGAGGCTCTGCACAACCACTACACGCAGAGAGCCCTCTCCCTGTCTCCGGGTAATAAGGGCCC (SEQ ID NO: 13)
ApaI
```

FIG. 2C-2

Ab T366W, Ia T366S:L368A:Y407V

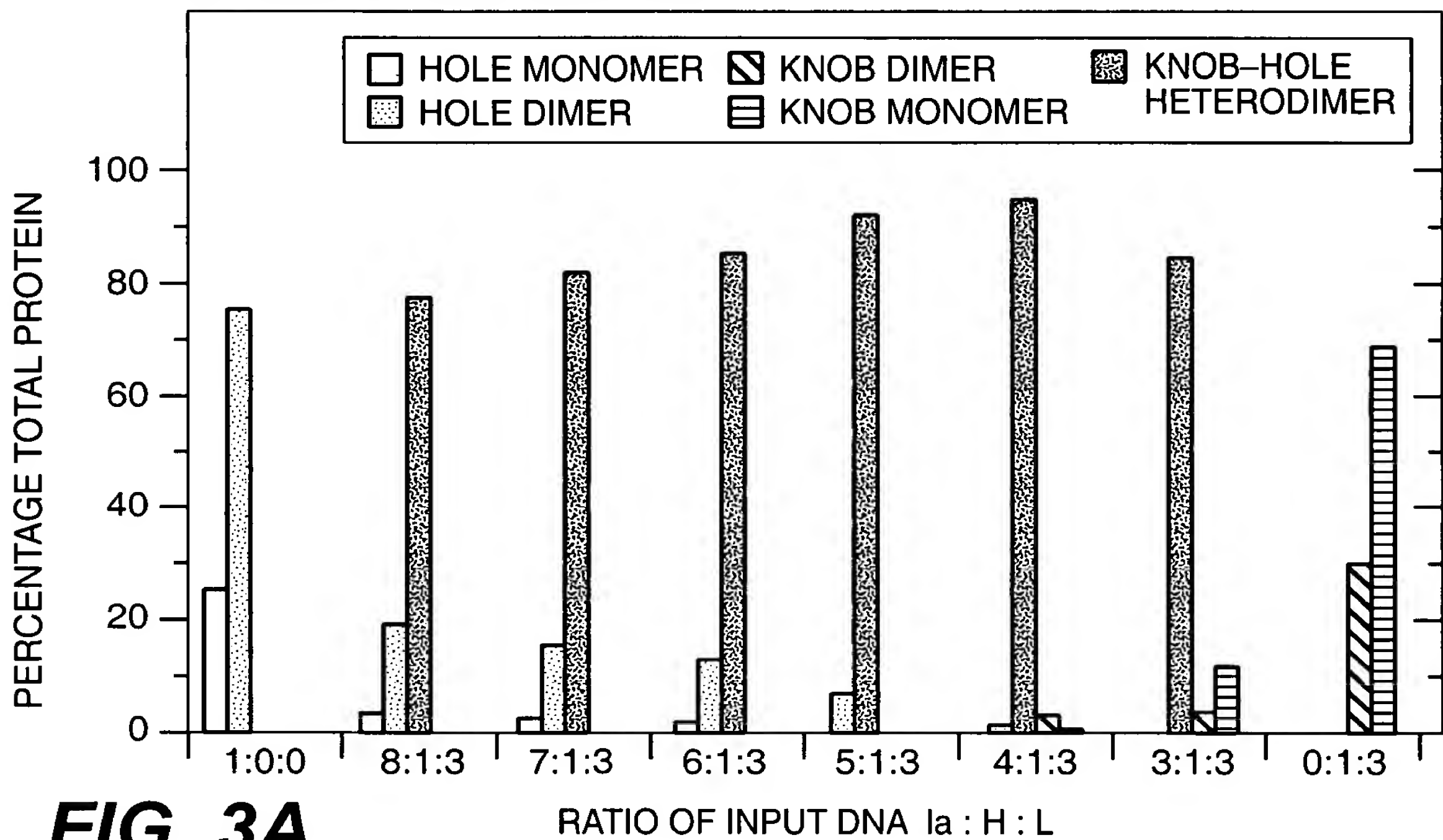


FIG. 3A

Ab T366W, Ia Y407A

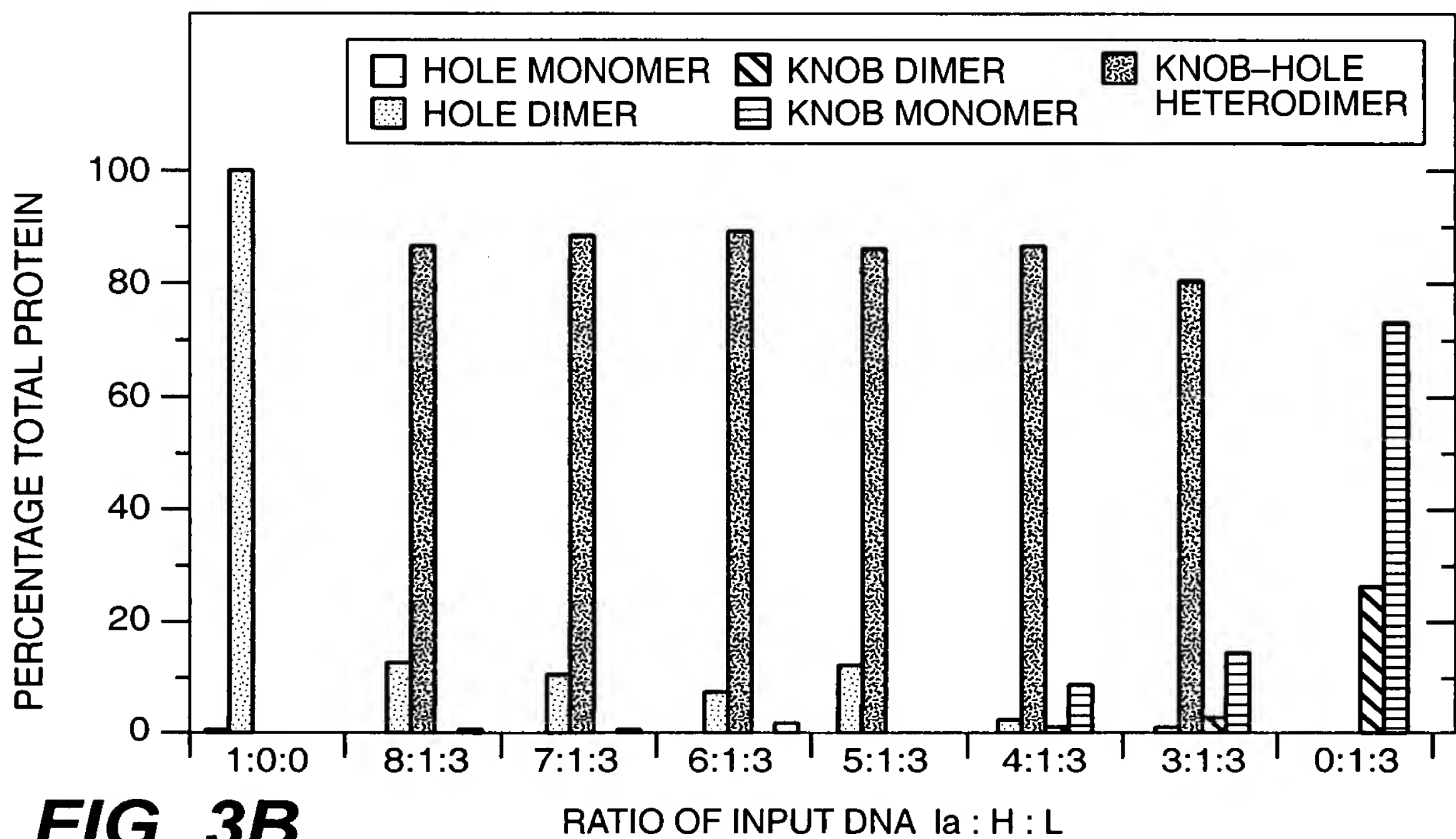
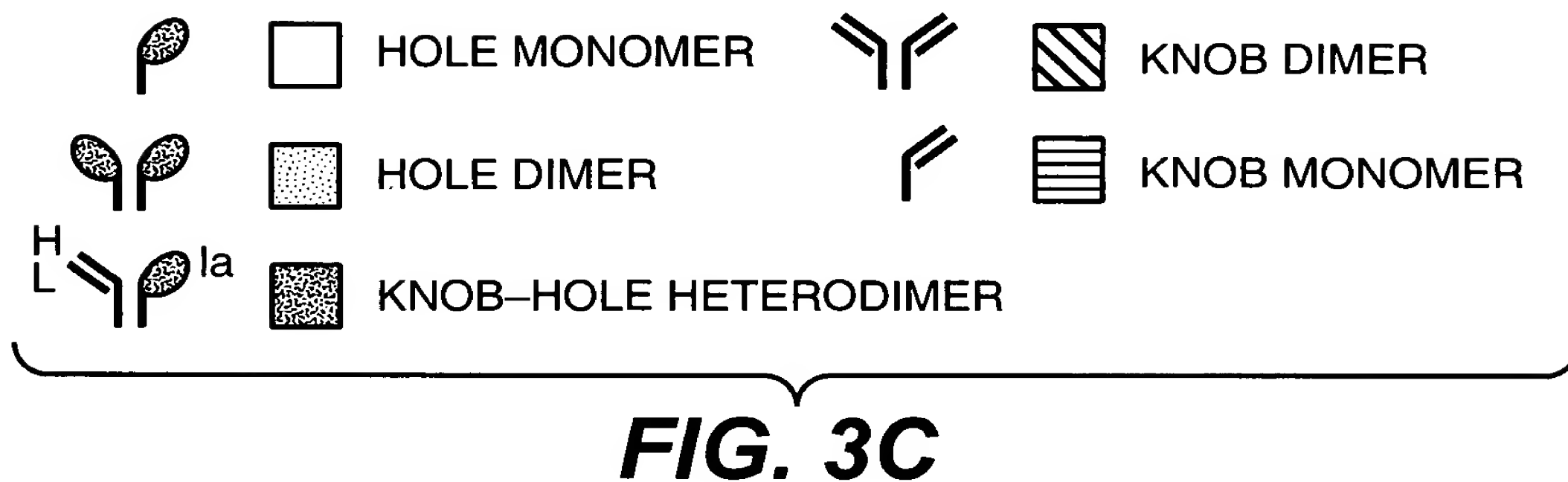


FIG. 3B



1 20 abc 30 40 50
Ax1.78 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV
Rse.23 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV
IGER.MAT2C1G11 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV
GCSFR.A4 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV
Rse.04 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV
obr.4 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV
Rse.20 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV
Rse.15 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV
vegf.5 QSVLTQPASVSGSPGQSIITISCTGTSSDVGGYNYSWYQQHPGKAPKLMIEGSKRPSGV

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CDR L1 CDR L2

60 70 80 90 a 100
Ax1.78 SNRFGSKSGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 14)
Rse.23 SNRFGSKSGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 15)
IGER.MAT2C1G11 SNRFGSKSGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 16)
GCSFR.A4 SNRFGSKSGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 17)
Rse.04 SNRFGSKSGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 18)
obr.4 SNRFGSKSGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 19)
Rse.20 SNRFGSKXGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 20)
Rse.15 SNRFGSKSGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 21)
vegf.5 SNRFGSKSGNTASLTISGLQAEDEADYCYSSYTRSTRVFGGGTKLTVL (SEQ ID NO: 22)

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CDR L3

FIG. 4

V_H

her3.18	10	20	30	ab	40	50	a
QVQLVQSGGGLVQPGGSLRLS	CAASGFTFS	SYEMN	--WVRQAPGK	GLEWVSGISGSGG	STYY		
*****	***	*	*	*	*	*	*
*****	***	*	*	*	*	*	*

obr.26

	CDR H1	CDR H2
EVQLVESGPG	SLTCTVSGGSISSGGYYWSWIRQHPGKLEWIGYIY-YSGSTYY	

60	70	80	abc	90	100	abcde	110
<u>ADSVKGRFTISRDN SKNTLYLQMNRLRAEDTAVYYCARDNGWELTDWYFDLWGRGTMVTVSS</u> (SEQ ID NO: 23)							
* * *	* * *	*	* * * * *		*	* * *	* * * *
<u>NPSLKSRVTISVDT SKNQFSLKLSVTAADTAVYYCARVDLEDYGSGASDYWGQGLVTVSS</u> (SEQ ID NO: 24)							
CDR H2				CDR H3			

V_L						
her3.18	10	20	<u>30</u>	40	50	60
DIQMTQSPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPKAPKLLIYKASSLASGAPSRRF						
obr.26			<u>CDR L1</u>		<u>CDR L2</u>	

70 80 90 100

SGSGSGTDTLTISLQPDFFATYYCQQYSNYPLTFGGGKLEIK (SEQ ID NO: 25)

CDR L3

FIG. 5

	H1	H2	H3	H4	H5	H6	H7	H8	H9	H10	H11
O1	49	47	51	81	60	48	76	51	100	62	51
O2	84	79	88	50	48	99	48	88	48	45	88
O3	83	82	85	51	50	95	49	85	49	46	85
O4	47	50	51	83	77	48	65	51	73	64	51
O5	49	47	51	81	60	48	76	51	100	62	51
O6	83	79	86	50	50	99	47	86	48	45	86
O7	81	100	86	51	49	80	48	86	47	44	86
O8	81	100	86	51	49	80	48	86	47	44	86
O9	81	100	86	51	49	80	48	86	47	44	86
O10	83	79	85	50	49	98	46	85	48	45	85
O11	83	80	87	50	49	99	47	87	48	45	87
O12	81	100	86	51	49	80	48	86	47	44	86
O13	49	47	51	81	60	48	76	51	100	62	51
O14	50	50	54	95	67	49	76	54	75	62	54
O15	82	79	85	49	48	97	46	85	47	44	85
O16	84	80	87	50	49	100	47	87	48	45	87
O17	45	44	47	65	62	45	62	47	62	100	47
O18	50	51	50	75	79	50	63	50	66	62	50

O1-O18: ANTI-Ob-R ANTIBODY CLONES obr. 1, 11, 12, 14, 15, 16, 17, 18, 19, 2, 20, 21, 22, 23, 24, 26, 3, 4, RESPECTIVELY.

H1-H11: ANTI-HER3 ANTIBODY CLONES her3.1, 3.10, 3.11, 3.12, 3.16, 3.18, 3.19, 3.22, 3.3, 3.4, 3.7, RESPECTIVELY.

FIG. 6